REMARKS

Reconsideration of this application, as amended, is respectfully requested.

I. Status of the claims

Claims 1-29, 67-77, 79, and 122-125 were pending in this case. Claim 29 has been cancelled without prejudice or disclaimer. The Applicants gratefully acknowledge that Examiner's finding that claim 125 is allowable. Applicants respectfully submit that the remaining claims in this application are allowable as well for reasons discussed below.

II. Rejections under 35 U.S.C. § 103 based on Chu and Shultz

Claims 1-3, 6-12, 16-28, 67-77, 79, and 122-124 were again rejected under 35 U.S.C. § 103(a) as being unpatentable over Chu et al. U.S. Patent no. 6,174,704 ("Chu") in view of Shultz U.S. Patent no. 6,242,235 ("Shultz"). The basis for the rejection is described on pages 3 and 4. Specifically, the Examiner states that Chu teaches compositions comprising aqueous solutions of alkylglycoside or alkylthioglycoside in amounts ranging from 0.5 to 5% w/v; that buffers such as TRIS or HEPES can be used to maintain a 7-8 pH value; that lysozyme can be included in the solutions; that the solutions can be used to prepare, extract, detect, purify and collect isolated proteins; that protein products can be incubated nickel charged resins and purified on resins; that the aqueous solutions may be used for lysing cells in a protein extraction process; and that octylthioglucosides can release proteins from cell membranes or cell walls. See pages 4 and 5 of the Office action. The Examiner then goes on to detail what is missing in Chu, namely the disclosure of inclusion of cationic surfactants comprising ethoxylated amine such as Tomah E-18-15 or Tomah E-18-5. The Examiner then uses Shultz to create the claimed composition from the prior art. On this basis, the Examiner alleges that the claimed composition is *prima facie* obvious in view of Shultz and Chu. The Applicants respectfully traverse this rejection.

Applicants stand by their reply in the previous response and submit that the section 103(a) rejection is based on improper hindsight reconstruction of the claimed invention based teachings in the Applicants' disclosure and not the cited art. Chu merely relates to lysis of host cells and extracting proteins of interest therefrom. See abstract. Specifically, Chu employs a reagent solution consisting essentially of an alkylglycoside or alkylthioglycoside. See col. 1, lines 51-55. Contrary to the Examiner's position, there is no teaching or suggestion in Chu that

any protein stabilization is necessary or even desirable to do. Indeed, Chu is completely silent with respect to a composition having "at least one surfactant having a hydrophobic-lipophilic balance value in the range from about 11 to about 16" and further in combination with "at least one cell membrane altering compound." See claims 1 and 67. A disclosure of a solution consisting essentially of alkylglycoside or alkylthioglycoside with added buffers and/or lysosyme is not a disclosure or suggestion of the composition and method as presently claimed. That Chu indicates, generally, that other constituents can be included which do not adversely affect the benefit's of Chu's solution can be included is not a suggestion that the presently recited surfactants would be useful in his composition. There is nothing in Chu that would provide an ordinary skilled artisan with any motivation to make the presently claimed composition with the expectation that such composition would provide the surprising and unexpected results discussed above. Shultz adds nothing that remedies the deficiencies in Chu's teachings.

Shultz merely relates to compositions for stabilizing proteins. Shultz does not teach or suggest that detergents of any type in the HLB range of about 11-16 and he is limited to cationic surfactants. There would be no incentive to select ANY surfactant in this HLB range in order to provide the composition or method of the present invention as presently claimed. Moreover, Shultz does not actually teach or suggest cell lysis nor does he teach or suggest that this would be necessary or desirable to do.

Selection of a material such as a surfactant to provide enzyme stability does not automatically presume that it will also provide effective lysis. Some surfactants can form micelles that may act to provide additional stabilization of cellular membrane proteins, thus making extraction more difficult. Accordingly, without a suggestion of lysis in Shultz, one of ordinary skill would not be motivated by Shultz's teachings concerning protein stabilization to include a surfactant (e.g., Tomah E-18-15 or E-18-5) in Chu's lysis reagent and thus arrive with the presently claimed invention with any reasonable expectation of success.

Applicants further submit that the claimed invention is not *prima facie* obvious over Chu in view of Shultz, because the instant application disclosed unexpected results for the claimed composition that are not taught or suggested in either of these references, alone or in combination. The instant application discloses the results of the levels of a reporter protein (luciferase) released from cells lysed by a cell membrane altering compound alone, by at least one surfactant alone, and by the combination of the two. The Applicants had discovered,

unexpectedly, that the presently claimed combination of a cell membrane altering compound and a surfactant having a hydrophilic-lipophilic balance value in the recited range yielded surprisingly superior results relative to the use of the membrane altering compound alone or the surfactant alone.

For instance, the application showed that cells treated with the combination of the membrane altering compound octyl-beta-thioglucopyranoside and at least one of surfactant yielded greater luciferase activity in the supernatant relative to the results obtained from cells treated with octyl-beta-thioglucopyranoside alone. As shown in Example 18, a comparison was made between solution no. 1 (octyl-beta-thioglucopyranoside only) with solution no. 3 (octyl-beta-thioglucopyranoside, Triton X-100 and Tomah E-18-15). It was discovered that solution no. 1 containing a cell membrane altering compound alone produced a very low light reading of 0.072/0.15, while solution no. 3 containing the combination of cell membrane altering compound and surfactant produced high light reading of 1639/1672. Similar results were obtained when solution no. 1 was compared with solution nos. 3 and 4.

Similarly, the application also demonstrated that, in the vast majority of the cases, cells treated with the combination of the cell membrane altering compound polymyxin B and the surfactant produced a surprising enhanced luciferase activity in the supernatant, relative to the results obtained from cells treated with the cell membrane altering compound alone. See, for instance, Example 3, where a comparison of results obtained from sample K with sample R. The results show that sample K (treated with polymyxin B alone) produced very low reading of 2.4/3.8, compared to sample R (treated with polymyxin B and Tomah E-18-15) which produced a high reading of 144/162. Similar results were obtained when sample K was compared with samples T, U, and O.

Additionally, the Applicants also discovered the surprising results were obtained for cells treated with the combination of at least one surfactant and the membrane altering compound octyl-beta-thioglucopyranoside, relative to cells treated with the surfactant alone. Cells treated with the claimed composition produced yielded a lysate with much greater luciferase activity relative to cells treated with the surfactant alone. See Example 17, where a comparison of results obtained from PRS No. 5 (the cell membrane altering compound alone) with PRS No. 6 (combination of the cell membrane altering compound with the surfactant) was made. The results showed that PRS no. 6 (containing Tomah E-18-15 and Triton X-100 alone) released only

5.81%/1.95% of lucifcrase into the supernatant, relative to PRS no. 5 (containing Tomah E-18-15, Triton X-100, and octyl-beta-thioglucopyranoside) released 95%/81% of luciferase into the supernatant. Similar results were obtained in a comparison between PRS No. 6 with Nos. 3 and 4.

Similarly, the Applicants also demonstrated that, in the vast majority of the cascs, cells treated with the combination of a surfactant and the membrane altering compound polymyxin B produced greater luciferase activity in thc supernatant than the results obtained from cells treated with the surfactant alone. In Example 3, for instance, a comparison was made between samples G with R. When sample G was treated with Tomah E-18-15 alone, a poor light reading of 2.58/2.11 was obtained, relative to sample R (treated with Tomah E-18-15 and polymyxin B) which produced a high reading of 144/162. Similar results were obtained when sample A was compared with sample L; sample, B compared with sample M; sample C compared with sample N; sample D compared with sample O; and sample E compared with sample P; and sample I compared with T.

In view of the above discussion, the Applicants submit that Chu and Shultz, either alone or in combination, does not teach or suggest the surprising results obtained by the claimed composition as taught by the instant application.

IV. Conclusion

In light of the above discussion and amendment, the Applicants submit that the claims are in allowable condition. A Notice to this effect is respectfully requested.

Reconsideration of this application is respectfully requested and a favorable determination is earnestly solicited. The Examiner is invited to contact the undersigned representative if the Examiner believes this would be helpful in expediting the allowance of this application.

Respectfully submitted,

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